

IN THE SPECIFICATION:

Please substitute the following amended paragraphs [0044] on page 12-13; paragraph [0090] on page 24 and paragraph [0187] on page 55, for the original paragraphs having the same paragraph numbers:

[0044] Figure 6: Sequence Comparison

Sequence alignment between human dihydrofolate reductase (DHFR) (Acc.# XM_165390 SEQ ID NO: 3) and the human eIF-5As (I: Acc.# NP_001961 (SEQ ID NO: 1); II: Acc.# NP_065123 (SEQ ID NO: 2)). Residues involved in the binding of the redox co-factor NADPH and of the molecular domains of folate (pterin, pABA, and glutamate) are indicated. The table summarizes the percent identity and similarity between the human DHFR and the human eIF-5As.

[0090] Similarly, optimized sequence alignment between human DHFR (Acc.# XM_165390 SEQ ID NO: 3) and the human eIF-5As (1: Acc.# NP_001961 (SEQ ID NO: 1); 2: Acc.# NP_065123 SEQ ID NO: 2)) revealed 37% identify/similarity with eIF-5A-I and 35% identify/similarity with eIF-5A-II. The N-terminal region of the human eIF-5As displays several isolated residues that in DHFR participate in binding of folate and the antifolate methotrexate (e.g. Ile⁷, Pro⁶¹, Arg⁷⁰), and of NADPH (e.g. Gly²⁰, Lys⁵⁴, Gly¹¹⁷, Ser¹¹⁸). Distinct sequence differences affecting residues involved in catalytic efficiency, such as the E30Q isolation, suggest the eIF-5As display limited if any DHFR activity, see Figure 6.

[0187] Example 5: Sequence Based Evidence for the Folate Region of eIF-5A

Optimized sequence alignment between human DHFR (Acc.# XM_165390 (SEQ ID NO: 3)) and the human eIF-5As (1: Acc.# NP_001961 (SEQ ID NO: 1); 2: Acc.# NP_065123 (SEQ ID NO: 2)) revealed 37% identify/similarity with eIF-5A-1 and 35% identify/similarity with eIF-5A-2. The N-terminal REGION of the human eIF-5As displays several isolated residues that in dihydrofolate reductase (DHFR) participate in binding of folate and methotrexate (e.g. Ile⁷, Pro⁶¹, Arg⁷⁰) and of NADPH (e.g. Gly²⁰,

Lys⁵⁴,Gly¹¹⁷,Ser¹¹⁸), whereas distinct differences, such as the E30Q isolocation, suggest limited DHFR activity, see Figure 6 (Hannauske-Abel, H. et al., Eur. J. Cancer 38, Supplement 7: S105, 2002).

Please enter the attached Sequence listing into the present application as filed.